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A comparison of APACHE II and CPIS scores for the prediction of 30-day mortality in patients with ventilator-associated pneumonia

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SUMMARY

Objective: The aim of this study was to compare the Acute Physiology and Chronic Health Evaluation II (APACHE II) score and the Clinical Pulmonary Infection Score (CPIS) for the prediction of 30-day mortality in patients with ventilator-associated pneumonia (VAP).

Methods: A single-center, prospective cohort study design was employed between January 1, 2010 and January 1, 2014. APACHE II and CPIS scores were determined on the day of VAP diagnosis. Discrimination was tested using receiver-operating characteristic (ROC) curves and the areas under the curve (AUC). Calibration was tested using the Hosmer–Lemeshow statistic.

Results: Of 135 patients with VAP, 39 died; the 30-day mortality was 28.9%. APACHE II and CPIS scores were significantly higher in non-survivors compared to survivors (23.1 ± 4.8 vs. 16.7 ± 4.6, $p < 0.001$; 6.8 ± 1.3 vs. 6.2 ± 1.3, $p = 0.016$). APACHE II had excellent discrimination for predicting 30-day mortality in patients with VAP, with AUC 0.808 (95% confidence interval (CI) 0.704–0.912, $p < 0.001$). However, the CPIS score did not have discrimination power for predicting mortality, with AUC 0.612 (95% CI 0.485–0.739, $p = 0.083$). The Hosmer–Lemeshow statistic showed good goodness-of-fit for observed 30-day mortality and APACHE II expected mortality (Chi-square = 1.099, $p = 0.785$). However, CPIS expected 30-day mortality did not fit the observed mortality (Chi-square = 6.72, $p = 0.004$).

Conclusions: These data suggest that APACHE II is useful for predicting 30-day mortality in patients with VAP, but that the CPIS does not have good discrimination and calibration for predicting mortality.

1. Introduction

Ventilator-associated pneumonia (VAP) is the most common nosocomial infection in patients receiving mechanical ventilation. The mortality rate of VAP patients ranges from 14% to as high as 70%.[1–3] Studies have confirmed that factors associated with mortality are malignancy, inappropriate initial treatment, bacteremia, acute respiratory distress syndrome/acute lung injury, shock, sepsis, disease severity, and the sepsis-related organ failure score.[1–4] Nevertheless, the accurate prediction of VAP mortality based on these risk factors remains difficult.

The Acute Physiology and Chronic Health Evaluation (APACHE) II is a severity-of-disease classification system. It was designed to measure the severity of disease for adult patients admitted to the intensive care unit (ICU).[5] It has been confirmed that APACHE II is a very useful instrument for the prediction of ICU mortality by the clinician.[6] The Clinical Pulmonary Infection Score (CPIS) was developed as a surrogate tool to facilitate the clinical diagnosis of VAP.[7] Studies have also found the CPIS to be an early clinical predictor of the outcome of VAP.[8,9] However, it is still not known which of these is the better tool for predicting mortality in patients with VAP.

The objective of this study was to evaluate and compare the predictive value of the APACHE II score and CPIS for 30-day mortality in patients with VAP.

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2. Methods

2.1. Study setting and design

This study was conducted at a university-affiliated hospital serving a population of 7.74 million.

A single-center, prospective cohort study design was employed between January 1, 2010 and January 1, 2014. The study was approved by the Medicine Human Studies Committee of the hospital, and the need for informed consent was waived.

Consecutive patients who stayed longer than 3 days in the respiratory intensive care unit (RICU) and who developed VAP were enrolled in the study. Patients younger than 18 years of age and those with another source of infection or a malignancy were excluded from the study.

2.2. Definition of VAP

VAP was defined based on a modification of the criteria established by the American College of Chest Physicians.[10] The criteria require the occurrence of new and persistent radiographic infiltrates in conjunction with two of the following: (1) a temperature >38.5 °C or < 36.5 °C; (2) a white blood cell count $>12 \times 10^9$/l or $<4 \times 10>^9$/l; and/or (3) purulent tracheobronchial secretions. Positive culture results from a protected specimen brush ($\geq 10^3$ CFU/ml), plugged telescopic catheter specimen ($\geq 10^3$ CFU/ml), bronchoalveolar lavage fluid specimen ($\geq 10^4$ CFU/ml), or quantitative endotracheal aspirate ($\geq 10^5$ CFU/ml) were also considered positive for the diagnosis of VAP.

2.3. Data collection

The APACHE II and the CPIS scores were determined on the day of VAP diagnosis. Demographic data, admission diagnosis of the patients, duration of mechanical ventilation, length of RICU and hospital stay, comorbidities, pathogens responsible for VAP, and 30-day mortality were also recorded.

2.4. Statistical analysis

First, the primary data analysis compared 30-day non-survivors with survivors. Continuous variables were compared using the Student's *t*-test for normally distributed variables. The Chi-square or Fisher's exact test was used to compare categorical variables. Second, the discrimination of non-survivors and survivors was tested using receiver-operating characteristic (ROC) curves and by evaluating the areas under the curve (AUC). APACHE II and CPIS were categorized into classes by selecting the best cut-offs. Third, calibration for comparing observed and predicted mortality was tested using the Hosmer–Lemeshow test. Logistic regression analysis was applied to estimate the predictive 30-day mortality of APACHE II and the CPIS. A two-tailed *p*-value of <0.05 was considered statistically significant. All analyses were performed using IBM SPSS Statistics version 19.0 (IBM Corp., Armonk, NY, USA).

3. Results

3.1. Patient characteristics

During the study period, 761 patients were admitted to the RICU and received mechanical ventilation. A total of 151 patients (19.8%) were diagnosed with VAP. Sixteen patients were excluded, 11 due to another source of infection and five due to malignancy, leaving 135 patients in the study cohort. Among these patients, 39 died within the 30 days after VAP diagnosis, giving a 30-day mortality of 28.9%. A flow diagram of the patients included in the study is given in Figure 1. The baseline characteristics of patients grouped by their survival status are provided in Table 1. APACHE II scores at the time of VAP diagnosis were significantly higher in non-survivors compared with survivors (23.1 ± 4.8 vs. 16.7 ± 4.6; $p < 0.001$). The CPIS were also significantly higher in non-survivors at the time of VAP diagnosis (6.8 ± 1.3 vs. 6.2 ± 1.3; $p = 0.016$).

3.2. Discrimination for 30-day mortality

The AUC for APACHE II predicting 30-day mortality in patients with VAP was 0.808 (95% confidence interval (CI) 0.704–0.912, $p < 0.001$); the AUC for CPIS was 0.612 (95% CI 0.485–0.739, $p = 0.083$). ROC curves for the two scoring systems for predicting 30-day mortality are shown in Figure 2. Table 2 shows the sensitivity and specificity values for the cut-off points of the two scoring systems. APACHE II >25 on the day of VAP diagnosis had high sensitivity (84.6%) and specificity (78.1%) in predicting mortality, but CPIS >7 had moderate sensitivity (74.4%) and low specificity (49.0%).

3.3. Calibration for 30-day mortality

Table 3 shows the observed mortality and the APACHE II score expected 30-day mortality for patients with VAP. Table 4 shows the observed mortality and CPIS expected mortality. The APACHE II expected 30-day mortality was 29.9% and the CPIS expected mortality was 35.9%. These are both higher than the observed actual 30-day mortality of 28.9%. The Hosmer–Lemeshow statistic showed good goodness-of-fit for observed 30-day mortality and the APACHE II expected mortality (Chi-square = 1.099, $p = 0.785$). However, the CPIS expected 30-day mortality did not fit the observed mortality (Chi-square = 6.72, $p = 0.004$). Calibration curves are shown in Figure 3.

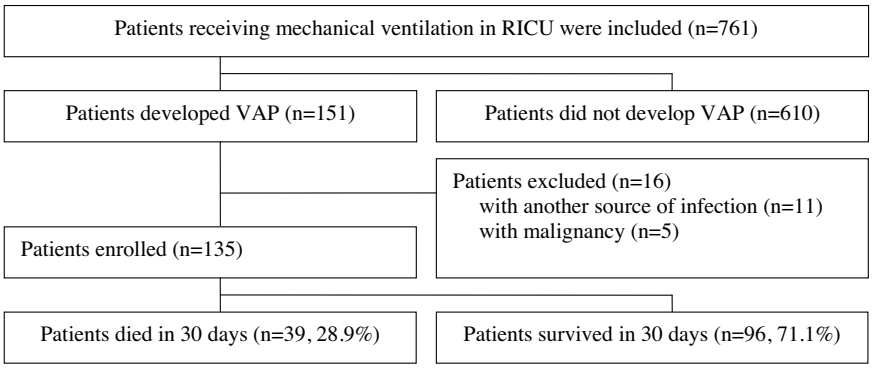

Figure 1. Flow diagram of patients included in the study.

Table 1
Baseline patient characteristics

Characteristics	30-day non-survivors ($n=39$)	30-day survivors ($n=96$)	p-Value
Age, years, mean ± SD	64.5 ± 12.7	62.4 ± 12.3	0.375
Gender, male/female	21/18	59/37	0.415
Admission diagnosis, COPD/non-COPD[a]	36/3	82/14	0.274
Comorbidities, n (%)			
Coronary artery disease	12 (30.8%)	21 (21.9%)	0.275
End-stage renal disease	2 (5.1%)	7 (7.3%)	0.648
Hepatic disease	2 (5.1%)	6 (6.3%)	0.802
Diabetes	3 (7.7%)	8 (8.3%)	0.902
Multidrug resistance, n (%)	31 (79.5%)	51 (53.1%)	0.004[b]
APACHE II, mean ± SD	23.1 ± 4.8	16.7 ± 4.6	<0.001[b]
CPIS, mean ± SD	6.8 ± 1.3	6.2 ± 1.3	0.016[b]

SD, standard deviation; COPD, chronic obstructive pulmonary disease; APACHE, Acute Physiology and Chronic Health Evaluation; CPIS, Clinical Pulmonary Infection Score.
[a] Non-COPD included community-acquired pneumonia, asthma, pulmonary embolism, and others.
[b] $p < 0.05$.

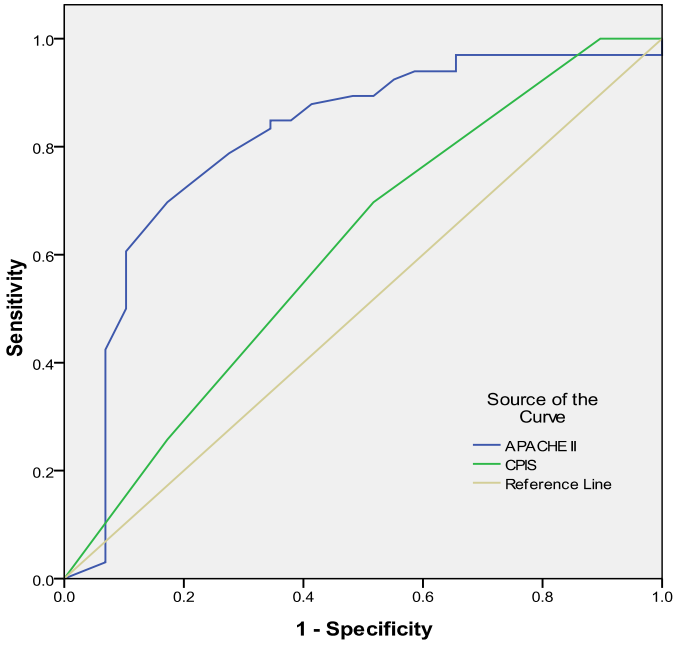

Figure 2. ROC curves for predicting 30-day mortality in patients with VAP (discrimination).

4. Discussion

We used discriminatory and calibrator power to compare the APACHE II and CPIS scores in predicting 30-day mortality in patients with VAP. Discrimination is the ability of the model to correctly separate the subjects into different groups. An AUC value of 0.5 indicates that the test has no discriminatory ability, whereas an AUC value of 1.0 indicates perfect diagnostic capability.[11] AUCs above 0.97 have been classified as excellent, between 0.93 and 0.96 as very good, between 0.75 and 0.92 as good, and less than 0.75 as obviously deficient in discriminatory accuracy.[12] Our study showed the AUC for APACHE II in predicting mortality to be 0.808 and the AUC for the CPIS to be 0.612. Our study also showed that an APACHE II score >25 had high sensitivity (84.6%) and specificity (78.1%) in predicting mortality. Calibration is the degree of correspondence between the estimated probability produced by the model and the actual observed probability. Although the APACHE II expected 30-day mortality of 29.9% was higher than the observed mortality of 28.9%, the Hosmer–Lemeshow statistic showed the APACHE II expected mortality to fit the observed mortality (Chi-square = 1.099, $p = 0.785$). A previous study has compared APACHE II, Sequential Organ Failure Assessment (SOFA), and CPIS scores in predicting the prognosis of patients with VAP; the researchers also found discrimination to be excellent for the APACHE II (AUC 0.81; $p = 0.001$) and deficient for the CPIS (AUC 0.63; $p = 0.069$).[13] Our results are in agreement with those of this previous study.

APACHE II, but not CPIS, showed good discrimination and calibration for predicting 30-day mortality in patients with VAP. We believe that the main reason for this is that the APACHE II was designed as a severity-of-disease classification and the CPIS was developed for the clinical diagnosis of VAP. APACHE II includes an acute physiology score, age points, and chronic health points.[5] The CPIS includes six parameters: temperature, white blood cell count, tracheal secretions, PaO_2/FiO_2, chest radiography, and microbiology.[7] These six parameters are directly related to infection. In our study, 39 patients (28.9%) died within 30 days after the diagnosis of VAP. Most of them died of multiple organ failure. Hence, 30-day mortality in patients with VAP must not be predicted by the CPIS. The CPIS may be a useful tool for predicting the attributable mortality of VAP. This could be confirmed in future studies.

Table 2
Four-fold table for predicting 30-day mortality with best cut-offs of the two scoring systems

	APACHE II (>25)		CPIS (>7)	
	Observed death	Observed survival	Observed death	Observed survival
Expected death	33	21	29	49
Expected survival	6	75	10	47
Sensitivity, %	84.6		74.4	
Specificity, %	78.1		49.0	

APACHE, Acute Physiology and Chronic Health Evaluation; CPIS, Clinical Pulmonary Infection Score.

Table 3
Observed mortality and APACHE II score expected 30-day mortality in patients with VAP

APACHE II category	Total	30-day non-survivors	30-day survivors	Observed mortality	Expected mortality
≤10	5	0	5	0.0%	6.4%
11–15	22	2	20	9.1%	10.5%
16–20	46	7	39	15.2%	18.1%
21–25	32	10	22	31.3%	35.6%
26–30	19	10	9	52.6%	54.1%
>30	11	10	1	90.9%	70.1%
Total	135	39	96	28.9%	29.9%

APACHE, Acute Physiology and Chronic Health Evaluation; VAP, ventilator-associated pneumonia.

Table 4
Observed mortality and CPIS expected 30-day mortality in patients with VAP

CPIS category	Total	30-day non-survivors	30-day survivors	Observed mortality	Expected mortality
≤4	0	0	0	0.0%	2.6%
5–6	32	4	28	12.5%	8.3%
7–8	33	11	22	33.3%	18.1%
9–10	48	14	34	29.2%	45.6%
10–12	22	10	12	45.4%	82.1%
Total	135	39	96	28.9%	35.9%

CPIS, Clinical Pulmonary Infection Score; VAP, ventilator-associated pneumonia.

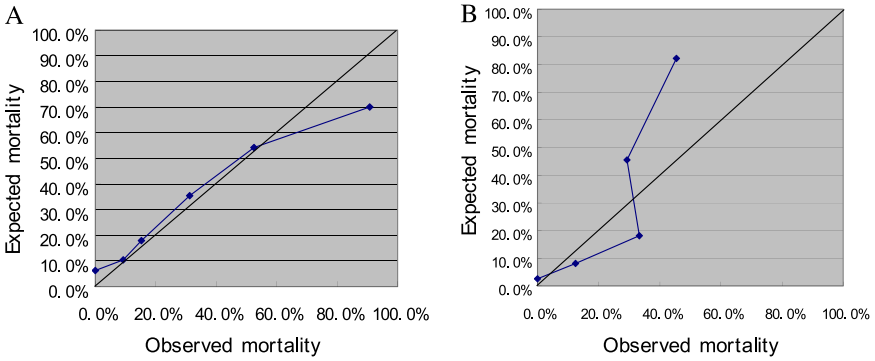

Figure 3. Calibration curves for predicting 30-day mortality in patients with VAP. The reference line represents perfect calibration. (A) APACHE II: the Hosmer–Lemeshow statistic showed good goodness-of-fit for observed 30-day mortality and the APACHE II expected mortality (Chi-square = 1.099, $p = 0.785$). (B) CPIS: the Hosmer–Lemeshow statistic showed the CPIS expected 30-day mortality did not fit the observed mortality (Chi-square = 6.72, $p = 0.004$).

In the present study, we also found non-survivors to have a significantly higher rate of multidrug-resistant organisms than survivors (79.5% vs. 53.5%, $p < 0.05$). This suggests that multidrug resistance may be a risk factor for 30-day mortality. We calculated multidrug resistance for predicting 30-day survival and found a sensitivity of 79.5% and specificity of 46.9%, with a Youden index of 0.264. Thirty-day mortality is affected by multiple factors. Multidrug-resistant organisms cannot explain the higher mortality alone. Multidrug-resistant organisms are not included in APACHE II. It is possible that the prediction power would be increased by combining APACHE II and multidrug resistance. This will be investigated in our next study.

An important limitation of this study was that we only compared APACHE II and CPIS scores, and found APACHE II to be useful in predicting VAP mortality. However APACHE II is inconvenient for use by practicing physicians as it requires the computation of multiple variables. Several simple scores have been developed to predict VAP mortality, such as the IBMP-10 score (Immunodeficiency, Blood pressure, Multilobar infiltrates, Platelet count, and 10-day hospitalization) and PIRO score (Predisposition, Infection, Response, and Organ failure).[14,15] We did not compare the APACHE II with these new scores in this prospective cohort. These can be verified in other studies.

In conclusion, our results suggest that the APACHE II score determined at the time of VAP diagnosis has good discriminatory and calibrator power to predict mortality in patients with VAP. However, the CPIS cannot be used as a tool to predict VAP mortality because of low discriminatory and calibrator power.

Conflict of interest/funding: None.

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